containing approximately 500 milligrams.

(*b*) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules in a high-speed glass blender with 1.0 milliliter of polysorbate 80 and sufficient 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3), to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Further dilute with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 0.5 microgram of novobiocin per milliliter (estimated).

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

[39 FR 19166, May 30, 1974, as amended at 50 FR 19921, May 13, 1985]

§ 455.170 Rifampin oral dosage forms.

§ 455.170a Rifampin capsules.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Rifampin capsules are gelatin capsules containing rifampin with a suitable and harmless filler and with or without binders, lubricants, and stabilizers. Each sample contains 150 milligrams or 300 milligrams of rifampin. Its potency is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of rifampin that it is represented to contain. Its loss on drying is not more than 3.0 percent. The rifampin used conforms to the standards prescribed by § 455.70(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The rifampin used in making the batch for potency, loss on drying, pH, absorptivity, identity, and crystallinity.

(*b*) The batch for potency and loss on drying.

(ii) Samples required:

(*a*) The rifampin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules into a high-speed glass blender jar containing 200 milliliters of methyl alcohol and blend for 3 minutes. Add 300 milliliters of 1 percent potassium phosphate buffer, pH 6.0 (solution 1), and blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 1 to the reference concentration of 5.0 micrograms of rifampin per milliliter (estimated).

(2) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

[39 FR 19166, May 30, 1974. Redesignated at 40 FR 53997, Nov. 20, 1975, and amended at 46 FR 46314, Sept. 18, 1981; 50 FR 19921, May 13, 1985]

§ 455.170b Rifampin-isoniazid capsules.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Rifampin-isoniazid capsules contain rifampin and isoniazid with a suitable and harmless filler and with or without binders, lubricants, and stabilizers in a gelatin capsule. Each capsule contains 300 milligrams of rifampin and 150 milligrams of isoniazid. Its rifampin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of rifampin that it is represented to contain. Its isoniazid content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of isoniazid that it is represented to contain. Its loss on drying is not more than 3.0 percent. The rifampin used conforms to the standards prescribed by § 455.70(a)(1). The isoniazid used conforms to the standards prescribed by the U.S.P.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The rifampin used in making the batch for potency, loss on drying, pH, absorptivity, identity, and crystallinity.

(*b*) The isoniazid used in making the batch for all U.S.P. specifications.

(*c*) The batch for rifampin content, isoniazid content, and loss on drying.

(ii) Samples required:

(*a*) The rifampin used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch: A minimum of 36 capsules.

(b) *Tests and methods of assay*—(1) *Rifampin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules into a high-speed glass blender jar containing 200 milliliters of methyl alcohol and blend for 3 minutes. Add 300 milliliters of 1 percent potassium phosphate buffer, pH 6.0 (solution 1), and blend for 3 to 5 minutes. Remove an aliquot and further dilute with solution 1 to the reference concentration of 5.0 micrograms of rifampin per milliliter (estimated).

(2) *Isoniazid content*—(i) *Equipment*—(*a*) *Electronic voltmeter.* A vacuum tube voltmeter or pH meter capable of measuring potentials from 0 to 1,400 millivolts.

(*b*) *Platinum electrodes.* Use twin platinum electrodes.

(*c*) *Constant current potential source.* Polarize the platinum electrodes by means of a battery and a suitable resistance in series with the electrodes, or by a stable electronic power supply, so that the current flow is about 2.5 microamperes.

(*d*) *Titration vessel.* Use a 100-milliliter beaker.

(ii) *Reagents*—(*a*) Concentrated hydrochloric acid, reagent grade.

(*b*) 0.1*N* Bromine solution. Dissolve 3.0 grams of potassium bromate and 15.0 grams of potassium bromide in sufficient water to make 1 liter. Preserve in dark amber-colored, glass-stoppered bottles.

(*c*) 1.0*N* Potassium iodide. Dissolve 16.5 grams of potassium iodide in 100 milliliters of water.

(*d*) Starch iodide paste, T.S. (U.S.P.).

(*e*) 0.1*N* Sodium thiosulfate (U.S.P.).

(*f*) 0.1*N* Hydrochloric acid.

(*g*) Chloroform, reagent grade.

(iii) *Standardization of 0.1N bromine solution.* Measure accurately about 25 milliliters of the bromine solution into a 500-milliliter iodine flask and dilute with 120 milliliters of water. Add 5 milliliters of hydrochloric acid, insert the stopper in the flask, and shake it gently. Then add 5 milliliters of potassium iodide T.S., insert the stopper, shake the mixture, and allow it to stand for 5 minutes. Titrate the liberated iodine with standard 0.1*N* sodium thiosulfate U.S.P., adding starch iodide paste T.S./U.S.P. as the endpoint is approached. Calculate the normality of the bromine solution.

(iv) *Preparation of sample solution.* Empty the contents of not less than 10 capsules into a tared weighing bottle. Mix and weigh the powder. Calculate the average capsule weight content and accurately weigh a sample equivalent to approximately 100 milligrams of isoniazid. Transfer the sample to a 125-milliliter separatory funnel. Add 20 milliliters of 0.1*N* hydrochloric acid and shake well. Extract the acidic solution with six 25-milliliter portions of chloroform, combining any interfacial emulsion with the aqueous phase throughout the extraction procedure. Discard the chloroform extracts. Quantitatively transfer the acidic aqueous layer to a 100-milliliter volumetric flask and dilute to volume with 0.1*N* hydrochloric acid.

(v) *Titration procedure.* Pipet 25 milliliters of the sample solution into the titration vessel and add 10 milliliters of concentrated hydrochloric acid. Adjust the volume to approximately 50 milliliters with water. Titrate potentiometrically at constant current with 0.1*N* bromine solution to a dead stop endpoint. Calculate the isoniazid content for the sample used and determine the isoniazid content for the average capsule weight as follows:

$$\frac{\text{Milligrams isoniazid per average capsule}}{} = \frac{V \times N \times 34.29 \times 4 \times W}{S}$$

where:

V=Volume in milliliters of 0.1*N* bromine solution used to titrate the sample;

N=Normality of bromine solution;

W=Average capsule weight content in milligrams;

S=Weight of sample in milligrams.

(3) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

[40 FR 53997, Nov. 20, 1975, as amended at 50 FR 19921, May 13, 1985]

§ 455.185 Vancomycin hydrochloride oral dosage forms.

§ 455.185a Vancomycin hydrochloride for oral solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Vancomycin hydrochloride for oral solution is vancomycin hydrochloride packaged in a suitable dispensing container. It may contain a suitable stabilizing agent. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of grams of vancomycin that it is represented to contain. Its moisture content is not more than 5 percent. When reconstituted as directed in the labeling, its pH is not less than 2.5 and not more than 4.5. The vancomycin hydrochloride used conforms to the standards prescribed by § 455.85.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assay on:

(*a*) The vancomycin hydrochloride used in making the batch for potency, moisture, pH, factor A content, and identity.

(*b*) The batch for potency, moisture, and pH.

(ii) Samples required:

(*a*) The vancomycin hydrochloride used in making the batch: 12 packages, each containing approximately 500 milligrams.

(*b*) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Empty the contents into an accurately measured volume of distilled water as directed in the labeling of the drug. Further dilute an aliquot with 0.1*M* passium phosphate buffer, pH 4.5 (solution 4), to the reference concentration of 10 micrograms of vancomycin per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the drug reconstituted as directed in the labeling.

[39 FR 19166, May 30, 1974, as amended at 50 FR 19921, May 13, 1985. Redesignated at 51 FR 22072, June 18, 1986, and amended at 59 FR 8399, Feb. 22, 1994]

§ 455.185b Vancomycin hydrochloride capsules.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Vancomycin hydrochloride capsules contain vancomycin hydrochloride dispersed in polyethylene glycol. Each capsule contains either 125 milligrams or 250 milligrams of vancomycin. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of vancomycin that it is represented to contain. Its moisture is not more than 8 percent. It passes the dissolution test. The vancomycin hydrochloride used conforms to the standards prescribed by § 455.85(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The vancomycin hydrochloride used in making the batch for potency, moisture, pH, factor A content, and identity.

(*b*) The batch for potency, moisture, and dissolution.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(*a*) The vancomycin hydrochloride used in making the batch: 12 packages, each containing approximately 500 milligrams.

(*b*) The batch: A minimum of 100 capsules.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules into a high-speed